

TITLE: Preparation of pyrimidine derivatives as drugs for treating disease and disorders of cerebral blood vessels

INVENTOR(S): Takatani, Takao; Takasugi, Hisashi; Kuno, Atsushi; Sugiyama, Yoshie; Sakai, Hiroyoshi; Okubo, Mitsuru

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 31 pp.  
CODEN: JKXXAF

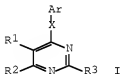
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63107966	A	19880512	JP 1987-124326	19870520 <--
PRIORITY APPLN. INFO.:			JP 1986-117800	A1 19860522 <--
OTHER SOURCE(S):		CASREACT 109:170451; MARPAT 109:170451		
ED		Entered STN: 12 Nov 1988		
GI				



AB The title compds. [I; Ar = (nitro or haloalkyl)aryl, fused benzene-heterocyclyl containing N or O; X = bond, lower hydroxyalkylene, lower alkenylene, NH, S, CO; R1 = (esterified) CO2H, lower hydroxyalkyl, lower haloalkyl, (N-substituted) CONH2 or lower aminoalkyl; R2 = H, lower alkyl; optionally R1R2 completing (substituted) N-containing heterocycle; R3 = aryl], were prepared as drugs e.g. for treating apoplexy. A mixture of 6-bromomethyl-4-(3-nitrophenyl)-2-phenyl-5-pyrimidinecarboxylic acid Me ester and Me2NCH2CHNH2 in iso-PrOH was stirred at 70° for 1 h to give 6-[2-(dimethylamino)ethyl]-4-(3-nitrophenyl)-5-oxo-2-phenyl-6,7-dihydropyrrolo[3,4-d]pyrimidine. The latter at 10 mg/kg i.p. extended the survival time of mice from 28.2 ± 1.1 s (control) to 33.6 ± 2.9 s when the mice were exposed to 100% N atmospheric

IC ICM C07D239-28  
ICS A61K031-505; C07D239-32; C07D239-42; C07D403-06; C07D413-04; C07D487-04

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1

IT 116904-45-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(acid chloride formation and amidation of, with methylpiperazine)

IT 116904-47-3  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(amidation of, with methylpiperazine)

IT 103311-82-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(bromination of)

IT 103294-21-9P 116904-11-1P 116904-12-2P 116904-13-3P  
116904-14-4P 116904-15-5P 116904-16-6P 116904-17-7P 116904-18-8P  
116904-19-9P 116904-20-2P 116904-21-3P 116904-22-4P 116904-23-5P

<u>116904-24-6P</u>	<u>116904-25-7P</u>	<u>116904-26-8P</u>
<u>116904-27-9P</u>	<u>116904-28-0P</u>	<u>116904-29-1P</u>
<u>116904-30-4P</u>	<u>116904-31-5P</u>	<u>116904-32-6P</u>
<u>116904-33-7P</u>	<u>116904-34-8P</u>	<u>116904-35-9P</u>
<u>116904-36-0P</u>	<u>116904-37-1P</u>	<u>116904-38-2P</u>
<u>116904-39-3P</u>	<u>116904-40-6P</u>	<u>116904-41-7P</u>
<u>116904-42-8P</u>	<u>116904-43-9P</u>	<u>116904-44-0P</u>
<u>116904-45-1P</u>	<u>116904-46-2P</u>	<u>116904-47-3P</u>
<u>116904-48-4P</u>	<u>116904-49-5P</u>	<u>116904-51-9P</u>
<u>116904-52-0P</u>	<u>116904-53-1P</u>	<u>116904-54-2P</u>
<u>116904-55-3P</u>	<u>116904-56-4P</u>	<u>116904-57-5P</u>
<u>116904-58-6P</u>	<u>116904-59-7P</u>	<u>116904-60-0P</u>
<u>116904-62-2P</u>	<u>116904-63-3P</u>	<u>116904-64-4P</u>
<u>116904-65-5P</u>	<u>116904-66-6P</u>	<u>116904-67-7P</u>
<u>116904-68-8P</u>	<u>116904-69-9P</u>	<u>116904-78-0P</u>
<u>116924-79-9P</u>	<u>116924-80-2P</u>	<u>117699-25-9P</u>

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as drug for treating apoplexy)

IT 62088-12-4P 70076-42-5P 116904-71-3P 116904-73-5P  
116904-75-7P 116904-76-8P 116904-77-9P

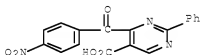
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, in preparation of drug for treating apoplexy)

IT 116904-45-1

RL: RCT (Reactant); RACT (Reactant or reagent)  
(acid chloride formation and amidation of, with methylpiperazine)

RN 116904-45-1 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-(4-nitrobenzoyl)-2-phenyl- (CA INDEX NAME)

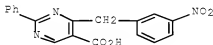


IT 116904-47-3

RL: RCT (Reactant); RACT (Reactant or reagent)  
(amidation of, with methylpiperazine)

RN 116904-47-3 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-[(3-nitrophenyl)methyl]-2-phenyl- (CA INDEX NAME)

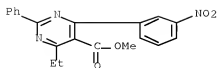


IT 103311-82-6

RL: RCT (Reactant); RACT (Reactant or reagent)  
(bromination of)

RN 103311-82-6 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-ethyl-6-(3-nitrophenyl)-2-phenyl-, methyl ester (CA INDEX NAME)

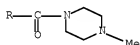
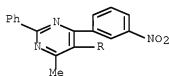


IT	<u>103294-21-9P</u>	<u>116904-25-7P</u>	<u>116904-26-8P</u>
	<u>116904-27-9P</u>	<u>116904-28-0P</u>	<u>116904-30-4P</u>
	<u>116904-31-5P</u>	<u>116904-34-8P</u>	<u>116904-35-9P</u>
	<u>116904-36-0P</u>	<u>116904-37-1P</u>	<u>116904-38-2P</u>
	<u>116904-39-3P</u>	<u>116904-40-6P</u>	<u>116904-41-7P</u>
	<u>116904-42-8P</u>	<u>116904-43-9P</u>	<u>116904-44-0P</u>
	<u>116904-45-1P</u>	<u>116904-47-3P</u>	<u>116904-48-4P</u>
	<u>116904-51-9P</u>	<u>116904-52-0P</u>	<u>116904-53-1P</u>
	<u>116904-54-2P</u>	<u>116904-55-3P</u>	<u>116904-56-4P</u>
	<u>116904-57-5P</u>	<u>116904-61-1P</u>	<u>116904-62-2P</u>
	<u>116904-63-3P</u>	<u>116904-64-4P</u>	<u>116904-65-5P</u>
	<u>116904-66-6P</u>	<u>116904-67-7P</u>	<u>116904-68-8P</u>
	<u>116904-69-9P</u>	<u>116904-78-0P</u>	<u>116924-79-9P</u>
	<u>116924-80-2P</u>		

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as drug for treating apoplexy)

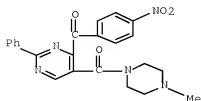
RN 103294-21-9 HCAPLUS

CN Methanone, [4-methyl-6-(3-nitrophenyl)-2-phenyl-5-pyrimidinyl] (4-methyl-1-piperazinyl)- (CA INDEX NAME)



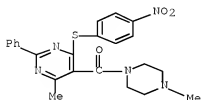
RN 116904-25-7 HCAPLUS

CN Piperazine, 1-methyl-4-[[4-(4-nitrobenzoyl)-2-phenyl-5-pyrimidinyl]carbonyl]- (9CI) (CA INDEX NAME)



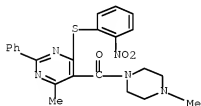
RN 116904-26-8 HCAPLUS

CN Methanone, [4-methyl-6-[(4-nitrophenyl)thio]-2-phenyl-5-pyrimidinyl](4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 116904-27-9 HCAPLUS

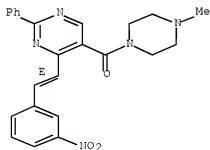
CN Methanone, [4-methyl-6-[(2-nitrophenyl)thio]-2-phenyl-5-pyrimidinyl](4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 116904-28-0 HCAPLUS

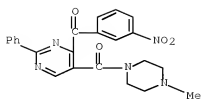
CN Piperazine, 1-methyl-4-[[4-[2-(3-nitrophenyl)ethenyl]-2-phenyl-5-pyrimidinyl]carbonyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



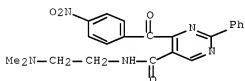
RN 116904-30-4 HCAPLUS

CN Piperazine, 1-methyl-4-[[4-(3-nitrobenzoyl)-2-phenyl-5-pyrimidinyl]carbonyl]- (9CI) (CA INDEX NAME)



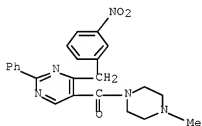
RN 116904-31-5 HCAPLUS

CN 5-Pyrimidinecarboxamide, N-[2-(dimethylamino)ethyl]-4-(4-nitrobenzoyl)-2-phenyl- (CA INDEX NAME)



RN 116904-34-8 HCAPLUS

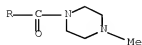
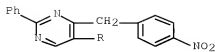
CN Methanone, (4-methyl-1-piperazinyl)[4-[(3-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl]-, hydrochloride (1:?) (CA INDEX NAME)



●x HCl

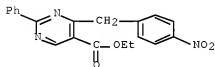
RN 116904-35-9 HCAPLUS

CN Methanone, (4-methyl-1-piperazinyl)[4-[(4-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl]- (CA INDEX NAME)



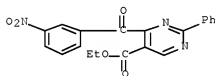
RN 116904-36-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-[(4-nitrophenyl)methyl]-2-phenyl-, ethyl ester (CA INDEX NAME)



RN 116904-37-1 HCAPLUS

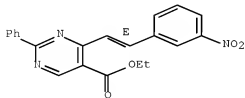
CN 5-Pyrimidinecarboxylic acid, 4-(3-nitrobenzoyl)-2-phenyl-, ethyl ester (CA INDEX NAME)



RN 116904-38-2 HCAPLUS

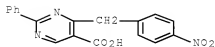
CN 5-Pyrimidinecarboxylic acid, 4-[2-(3-nitrophenyl)ethenyl]-2-phenyl-, ethyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 116904-39-3 HCAPLUS

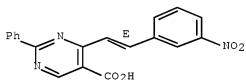
CN 5-Pyrimidinecarboxylic acid, 4-[(4-nitrophenyl)methyl]-2-phenyl- (CA INDEX NAME)



RN 116904-40-6 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-[2-(3-nitrophenyl)ethenyl]-2-phenyl-, (E)- (9CI) (CA INDEX NAME)

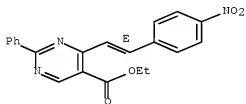
Double bond geometry as shown.



RN 116904-41-7 HCAPLUS

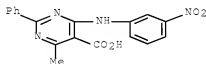
CN 5-Pyrimidinecarboxylic acid, 4-[2-(4-nitrophenyl)ethenyl]-2-phenyl-, ethyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



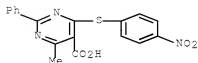
RN 116904-42-8 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-methyl-6-[(3-nitrophenyl)amino]-2-phenyl- (CA INDEX NAME)

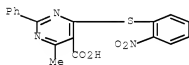


RN 116904-43-9 HCAPLUS

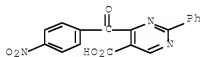
CN 5-Pyrimidinecarboxylic acid, 4-methyl-6-[(4-nitrophenyl)thio]-2-phenyl-  
(CA INDEX NAME)



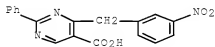
RN 116904-44-0 HCAPLUS  
CN 5-Pyrimidinecarboxylic acid, 4-methyl-6-[(2-nitrophenyl)thio]-2-phenyl-  
(CA INDEX NAME)



RN 116904-45-1 HCAPLUS  
CN 5-Pyrimidinecarboxylic acid, 4-(4-nitrobenzoyl)-2-phenyl- (CA INDEX NAME)

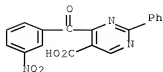


RN 116904-47-3 HCAPLUS  
CN 5-Pyrimidinecarboxylic acid, 4-[(3-nitrophenyl)methyl]-2-phenyl- (CA INDEX NAME)



RN 116904-48-4 HCAPLUS  
CN 5-Pyrimidinecarboxylic acid, 4-(3-nitrobenzoyl)-2-phenyl- (CA INDEX NAME)

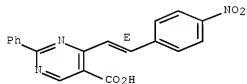




RN 116904-51-9 HCAPLUS

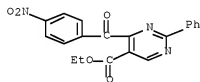
CN 5-Pyrimidinecarboxylic acid, 4-[2-(4-nitrophenyl)ethenyl]-2-phenyl-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



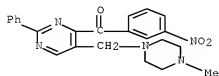
RN 116904-52-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-(4-nitrobenzoyl)-2-phenyl-, ethyl ester (CA INDEX NAME)



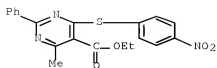
RN 116904-53-1 HCAPLUS

CN Methanone, [5-[(4-methyl-1-piperazinyl)methyl]-2-phenyl-4-pyrimidinyl](3-nitrophenyl)- (CA INDEX NAME)



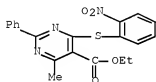
RN 116904-54-2 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-methyl-6-[(4-nitrophenyl)thio]-2-phenyl-, ethyl ester (CA INDEX NAME)



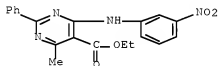
RN 116904-55-3 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-methyl-6-[(2-nitrophenyl)thio]-2-phenyl-, ethyl ester (CA INDEX NAME)



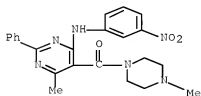
RN 116904-56-4 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-methyl-6-[(3-nitrophenyl)thio]-2-phenyl-, ethyl ester (CA INDEX NAME)



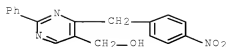
RN 116904-57-5 HCAPLUS

CN Methanone, [4-methyl-6-[(3-nitrophenyl)amino]-2-phenyl-5-pyrimidinyl] (4-methyl-1-piperazinyl)- (CA INDEX NAME)



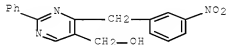
RN 116904-61-1 HCAPLUS

CN 5-Pyrimidinemethanol, 4-[(4-nitrophenyl)methyl]-2-phenyl- (CA INDEX NAME)



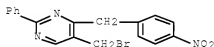
RN 116904-62-2 HCAPLUS

CN 5-Pyrimidinemethanol, 4-[(3-nitrophenyl)methyl]-2-phenyl- (CA INDEX NAME)



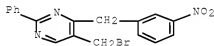
RN 116904-63-3 HCAPLUS

CN Pyrimidine, 5-(bromomethyl)-4-[(4-nitrophenyl)methyl]-2-phenyl- (CA INDEX NAME)



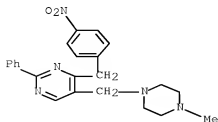
RN 116904-64-4 HCAPLUS

CN Pyrimidine, 5-(bromomethyl)-4-[(3-nitrophenyl)methyl]-2-phenyl- (CA INDEX NAME)



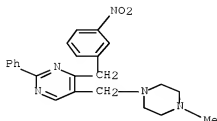
RN 116904-65-5 HCAPLUS

CN Pyrimidine, 5-[(4-methyl-1-piperazinyl)methyl]-4-[(4-nitrophenyl)methyl]-2-phenyl- (CA INDEX NAME)



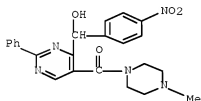
RN 116904-66-6 HCAPLUS

CN Pyrimidine, 5-[(4-methyl-1-piperazinyl)methyl]-4-[(3-nitrophenyl)methyl]-2-phenyl- (CA INDEX NAME)



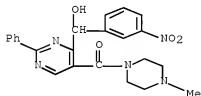
RN 116904-67-7 HCAPLUS

CN Methanone, [4-[hydroxy(4-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl] (4-methyl-1-piperazinyl)- (CA INDEX NAME)



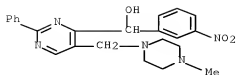
RN 116904-68-8 HCAPLUS

CN Methanone, [4-[hydroxy(3-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl] (4-methyl-1-piperazinyl)- (CA INDEX NAME)



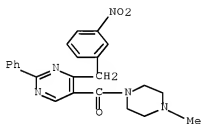
RN 116904-69-9 HCAPLUS

CN 4-Pyrimidinemethanol, 5-[(4-methyl-1-piperazinyl)methyl]- $\alpha$ -(3-nitrophenyl)-2-phenyl- (CA INDEX NAME)



RN 116904-78-0 HCAPLUS

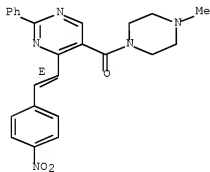
CN Methanone, (4-methyl-1-piperazinyl) [4-[(3-nitrophenyl)methyl]-2-phenyl-5-pyrimidinyl]- (CA INDEX NAME)



RN 116924-79-9 HCAPLUS

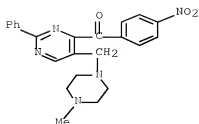
CN Piperazine, 1-methyl-4-[[4-[2-(4-nitrophenyl)ethenyl]-2-phenyl-5-pyrimidinyl]carbonyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 116924-80-2 HCAPLUS

CN Methanone, [5-[(4-methyl-1-piperazinyl)methyl]-2-phenyl-4-pyrimidinyl] (4-nitrophenyl)- (CA INDEX NAME)

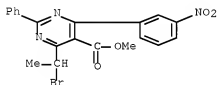


IT 116904-73-5P 116904-77-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, in preparation of drug for treating apoplexy)

RN 116904-73-5 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-(1-bromoethyl)-6-(3-nitrophenyl)-2-phenyl-,  
methyl ester (CA INDEX NAME)



RN 116904-77-9 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-methyl-2-phenyl-6-[3-  
(trifluoromethyl)phenyl]-, methyl ester (CA INDEX NAME)

